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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
07/839,194	02/20/1992	KATHERINE GORDON	IG5-4.4	6108

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	07/839,194	GORDON ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-9,11,16,17,19-22 and 24-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5-9, 11, 16, 17, 19-22, 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a divisional of 07/441,785, filed 11/27/1989, now ABN, which is a divisional of 06/849,815, filed 04/09/1986, now ABN.

Please note that the Examiner of record and art unit has changed. The Examiner of record is now **Joseph T. Woitach** and the group art unit is now **1632**.

Applicants appeal brief filed March 23, 2003 has been received and entered.

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's Appeal Brief submission after final filed on March 23, 2003 has been entered. New grounds of rejection not previously made of record are set forth below.

Claims 1, 2, 5-9, 11, 16, 17, 19-22, 24-29 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5-9, 11, 16, 17, 19-22, 24-29 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

The appeal brief filed March 23, 2003 provides essentially the same arguments provided in 07/938,322, now US Patent 7,045,676. Upon further consideration of the instant prosecution and the decision of the board (see action mailed July 25, 2003 in 7,045,676) regarding the merits of the basis of the rejection, it has been decided that it would not constitute an undue burden for enablement to isolate promoter sequences of milk proteins. Further, the evidence of record and arguments demonstrate that the 5' end of some genes from some species encoding milk proteins were known at the time of filing, and preliminary and routine characterization of said sequences identified transcriptional elements such as the TATA and CAT boxes (see Table 1, pages 14-15 of the appeal brief) provide adequate teaching and structural evidence for meeting the requirement of written description.

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claim 19 is not an original claim, and upon review for support of the invention as claimed it is found that the phrase "a sequence upstream from the transcriptional start site of a mammalian milk protein which includes a milk protein promoter" is new matter because it

broadens the scope of the invention disclosed in the instant specification. The recitation is interpreted to encompass any fragment of sequence upstream of a transcriptional start site of a milk protein. The specification provides for the use of milk protein promoters, and that such promoters are found upstream or at the 5' end of sequences encoding the protein, however beyond this description which generally applies to a promoter of any gene, the specification fails to describe or contemplate fragments or combination of fragments that provide transcriptional control. The thrust of the guidance of the present disclosure is for the use of mammary gland specific promoters to express genes of interest in mammals. To this end, promoters are generally discussed, and more specifically how to isolate milk protein promoters are generally provided, however there is no description nor guidance beyond isolating the sequence 5' to the transcriptional start site supporting the isolation, identification and characterization of elements within a promoter now encompassed by claim 19. The specification fails to provide any description of such functional fragment sequences, and at the time of filing the art of record fails to demonstrate that they were readily known species of transcriptional elements for milk protein promoters. Again, it is noted that this is a new matter rejection with respect to support for the embodiment of providing transcriptional control using any sequence upstream the transcriptional start site of a milk protein.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to

include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 5-9, 11, 16, 17, 19-22, 24-29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,727,405. Although the conflicting claims are not identical, they are not patentably distinct

from each other because the DNA constructs instantly claimed have the one enabled use in making transgenic non-human mammals of claims 1-4, and are anticipated by the DNA construct of claim 5. Claim 5 of '405 recites and encompasses a whey acidic protein promoter which was one of the mammalian milk protein promoter sequences instantly disclosed and encompassed by the breadth of the claims, and one of the few specifically disclosed and known at the time of filing. Embodiments of the dependent claims instantly set forth, such as that the secretion sequence is from the protein of interest or that it is cleaved from the secreted protein are inherent properties of secreted proteins/signal sequences, and obvious embodiments for heterologous secretion signal sequences. Embodiments that the construct comprise a transcriptional stop sequence or a polyadenylation sequence are obvious and necessary components of an expression vector for expression of any protein of interest.

Claims 1, 2, 5-9, 11, 16, 17, 19-22, 24-29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-41 of U.S. Patent No. 7,045,676. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of producing a protein recite and require the same DNA construct instantly claimed. The instantly claimed DNA construct has essentially one use in view of the teachings of the present specification, that being in generating a transgenic mammal in which the DNA construct provides for expression of a gene of interest in said lactating mammal. Dependent claims in '676 set forth specific embodiments of the DNA construct that is used in the method that mirror the dependent claims for the DNA construct instantly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 5-9, 11, 16, 17, 19-22, 24-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically,

Independent claims 1 and 19 recite that the mammalian milk protein promoter sequence used "does not naturally control transcription". The metes and bounds of what is considered "natural" are indefinite because this is not an art accepted term, and what this embodiment encompasses or how it is determined is not set forth in the instant specification. Literal support for the embodiment in the instant specification is noted, however it does not provide for a sufficient definition of what "natural" encompasses. It is unclear to how similar or to how different expression of this element would have to be and be considered a natural control of transcription, which is required by the claim in the control of the gene of interest. Since the terminology is not art accepted and the specification fails clearly set forth the metes and bounds of the claims, the claims are considered indefinite. Dependent claims are included in the basis of the rejection because they fail to clarify and clearly set forth any specific metes and bounds to the independent claims. While it is noted that claims 17 and 22 do recite the "α-lactalbumin" promoter, the claims fail to clearly set forth what would be considered a natural control/level of expression of even this specific promoter.

Claims 8 and 27 are indefinite in the recitation of "derived from SV40 virus DNA" because how similar or different defining the metes and bounds of the claimed sequence is from SV40 is not clearly set forth.

Claim 19 is confusing and indefinite in the recitation of "a sequence upstream form the transcriptional start site of a mammalian milk promoter which includes a milk protein promoter". As recognized in the art and acknowledged in the teaching of the present specification, promoter elements are identified as the 5' sequence before the transcriptional start site. The phrase "which includes a milk protein promoter" is vague and confusing in how it limits the portion of the claim preceding it, or what it's recitation is intended to encompass with respect to the metes and bounds of the claim. In addition to issues discussed above about the functional requirements of the sequence "naturally" controlling transcription encompassed by the claim, the claim is unclear to what "a sequence" would structurally require to meet the limitations of the claim. For example, some characterized milk promoters known at the time of filing contain TATA boxes which naturally control transcription, and in this case, it is unclear if the claim intends to exclude such elements since they do not include sequences that "naturally control". Dependent claims are included in the basis of the rejection because they fail to clarify and clearly set forth any specific metes and bounds to the independent claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5-9, 16, 17, 19-22, 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Qasba *et al.* (Nature, March 1984).

Claim 1 encompasses a DNA construct and sets forth three structural elements comprised on the construct: a mammalian milk protein promoter, a gene of interest operatively linked to said promoter, and a sequence encoding a secretion signal operatively linked to the gene of interest. The functional property of the promoter encompassed by the claim requires that it does not naturally control transcription of the gene of interest, and one reasonable interpretation would be any promoter that provides for an expression profile that is different from that "naturally" found *in vivo*. In this case, a genomic fragment comprising a fragment of a milk protein promoter and a corresponding sequence that encodes a protein of interest would anticipate this functional requirement since the promoter fragment does not provide for the same expression profile "naturally" provided by the entire intact promoter found in the genome. Independent claim 19 is less defining with respect to the promoter, encompassing "a sequence upstream form the transcriptional start site of a mammalian milk promoter which includes a milk protein promoter" which can reasonably be interpreted to encompass effectively any functional fragment of a milk promoter including elements as simple as a TATA or CAT box.

Qasba *et al.* teach a DNA sequence of the rat α-lactalbumin comprising 1247 bases of the promoter containing a TATA box (page 379) linked to the entire coding sequence for the secreted protein lactalbumin. The specific DNA sequence identifying the 1247 base pair 5' end, a 19 amino acid secretion signal, and a lactalbumin encoding sequence is set forth in figure 1. Dependent claims set require that the DNA contain a polyadenylation signal, more specifically reciting that it is derived from SV40, which can reasonably be interpreted to be effectively any

polyadenylation sequence as well as other construct elements. Qasba *et al.* teach that the DNA sequence contains a AATAAA polyadenylation sequence at the 3' end, as well as a transcriptional stop signal at position 3762 (see legend for figure 1, page 379).

Claims 19-22, 24-28 are rejected under 35 U.S.C. 102(a) as being anticipated by Cilibero *et al.* (Cell, June 1985).

The breadth of the claims are discussed above. With respect to claim 19, it is noted that a reasonable interpretation of the scope of the claim requires only "**a** sequence upstream from the transcriptional start site of a mammalian milk protein" and encompasses any heterologous promoter which contains transcriptional elements of a milk protein promoter such as TATA and CAT boxes. Cilibero *et al.* teach an DNA construct which expresses the secreted protein α1-antitrypsin (see figure 2 for the map of two complete lambda clones of α1-antitrypsin). It is noted that the promoter used by Cilibero *et al.* is the α1-antitrypsin promoter, which is not a milk protein, however the promoter disclosed is described and does contain TATA and CAAT boxes also found in milk protein promoters(see page 533, first column and figure 3). Since such promoter sequences are effectively indistinguishable with respect to the source from which they are derived, the TATA and CAAT boxes of the α1-antitrypsin promoter are considered to anticipate the structural requirements of a TATA or CAAT box from a milk protein promoter.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Pittius *et al.* PNAS 85:5874-5878 (August 1988) provides further evidence, such as that found in Andres *et al.* (PNAS, 1987-of record) that milk/mammary gland specific promoters known at the time of filing could successfully be used to generate transgenic mice for the expression of a hetelogous protein, however that the use of such promoters resulted in the expression in other unrelated tissues such as the brain, toungue, kidney and sublingual gland of the transgenic animal (see summary in abstract).

Conclusion

No claim is allowed.

Claims 11 and 29 are free of the art of record because while the coding sequences for human tPA and hepatitis B surface antigens, and the promoter sequences for mammalian milk protein promoters where known at the time of filing, and that only routine molecular biology techniques would be required to successfully link these specific elements into one DNA construct, the art fails to provide adequate motivation for the combination of promoter and gene product.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach